

CPS Insider is a quarterly client newsletter produced by the University of Massachusetts Medical School (UMMS) Clinical Pharmacy Services (CPS).

## 1-2 Drug Watch

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## At a Glance



### Noteworthy

FDA against approving an over-the-counter statin



### Heads Up!

Topics for the Upcoming Issue: CPS' plan for clinical programming

## New Generics

- **Omeprazole (Prilosec®)**  
Approved 12/4/2007
- **Oxcarbazepine (Trileptal®)**  
Approved 10/9/2007  
Launched 10/10/2007

## Rx to OTC

- **Zyrtec-D® (cetirizine/pseudoephedrine)**  
Approved 11/9/2007  
Launched after 1/2008  
Formulation: Tablet
- **Zyrtec® (cetirizine)**  
Approved 11/21/2007  
Launched after 1/2008  
Formulation: tablet, chewable tablet, solution

## Drug Watch

New To Market

### Isentress® (raltegravir)

Approved: 10/12/2007

Manufacturer: Merck & co

Formulation: Tablet

Raltegravir is an oral, first-in-class HIV-1 integrase inhibitor. More specifically, raltegravir prevents the insertion of HIV DNA into the human genome.

Raltegravir received accelerated approval through the FDA for the treatment of HIV-1 infection in combination with other antiretroviral agents in treatment-experienced adult patients with multidrug-resistance.

The recommended dose of raltegravir is 400mg twice daily. The most common adverse events include headache, pyrexia, nausea and diarrhea.

Due to reduced plasma concentrations of raltegravir, caution should be used during the co-administration of strong inducers of uridine diphosphate glucuronosyl-transferase 1A1 (e.g. rifampin).

New To Market

### Bystolic® (nebivolol)

Approved: 12/17/2007

Manufacturer: Forest Labs/Mylan

Formulation: Tablet

Nebivolol is a  $\beta$ -adrenergic receptor blocking agent that is preferentially  $\beta_1$  selective. At doses <10 mg per day, nebivolol has the added pharmacological properties of producing vasodilation and reducing total peripheral resistance. Importantly, at higher doses and in poor metabolizers, both  $\beta_1$  and  $\beta_2$  adrenergic receptors may be inhibited. Definitive antihypertensive responses have not been established, however, involved factors may include decreased heart rate, decreased myocardial contractility, diminution of tonic sympathetic outflow, suppression of renin activity, vasodilation, and decreased peripheral vascular resistance.

Nebivolol is FDA-approved for the treatment of hypertension when used alone or in combination with other antihypertensive agents. The recommended starting dose of nebivolol is 5mg once daily, and doses may be increased at 2-week intervals up to 40mg daily. The most common adverse events include headache, fatigue, dizziness, diarrhea, bradycardia, and nausea.

Due to a potential risk of bradycardia, caution should be taken with concomitant use of myocardial depressant agents or inhibitors of atrioventricular conduction. Also, combination use of nebivolol and CYP2D6 inhibitors may result in increased plasma levels of nebivolol (e.g. fluoxetine).

## New FDA-Approved Indications

- **Menactra® (bacterial meningitis vaccine)**  
Approved on **10/18/2007**. Expanded approval includes children 2 to 10 years of age for protection against meningococcal disease.
- **Abilify® (aripiprazole)**  
Approved on **10/29/2007**. Approved for adjunct treatment to antidepressants for major depressive disorder in adults.
- **Crestor® (rosuvastatin)**  
Approved on **11/8/2007**. For slowing the progression of atherosclerosis as part of a treatment strategy to lower total cholesterol and LDL cholesterol as an adjunct to diet.

## New Formulations and Dosages

- **SymlinPen® (pramlintide)**  
SymlinPen® 60 delivers 15, 30, 45, or 60 µg/dose; SymlinPen® 120 delivers 60 or 120 µg/dose  
Approved 10/1/2007
- **Nifeipine XL**  
90mg tablet (generic)  
Approved 10/3/2007
- **Voltaren® (diclofenac)**  
1% topical gel  
Approved 10/17/2007
- **Hydrocodone bitartrate/ibuprofen**  
2.5mg/200mg tablet (generic)  
Approved 10/19/2007

Information available at: [www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm](http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm)



## Clinical Notes

### NATIONAL ASTHMA EDUCATION AND PREVENTION Program (NAEPP) – 2007

#### Revisions

##### Managing Asthma Long Term: Selected Key Points

- Recommendations for asthma management in children 0-4 and 5-11 years of age are presented separately from recommendations for managing asthma in children ≥12 years of age and in adults.
- Consider recommending long-term therapy for children 0-4 years of age to reduce impairment and risk of exacerbations in infants and young children who had >4 wheezing episodes in the past year that lasted >1 day and affected sleep AND who have risk factors for developing persistent asthma.

##### Treatment Options: Selected Key Points

- Inhaled corticosteroids (ICSs) are the preferred therapy for initiating long-term control therapy in children of all ages and they are generally safe for long term use at low doses.
- For patients 0-4 years of age inadequately controlled on low-dose ICS, increasing the dose of ICSs to medium dose is recommended before adding adjunctive therapy.
- For patients children 5-11 years of age, youths ≥12 years of age, and adults inadequately controlled on low dose ICSs, increasing the dose of ICS to a medium dose or adding adjunctive therapy to a low dose of ICS are considered equal options.

For more information on the 2007 NAEPP guideline, please visit: [www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf](http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf)

### Recommendations of the advisory committee on immunization practices (ACIP) – 2007-2008

#### Revisions

##### Influenza Prevention & Control Recommendations:

- Children 6 months to 8 years of age should initially receive 2 doses of trivalent inactivated influenza vaccine (TIV) administered ≥1 month apart.
- Live, attenuated influenza vaccine (LAIV), Flumist® is now FDA-approved for children as young as 2 years of age.
- As an alternative to TIV, LAIV may be administered to children 2 to 8 years old with 2 doses administered ≥6 weeks apart.
- Children receiving only 1 dose of the influenza vaccine in their first year of vaccination should receive 2 doses in the immediately following year.
- In addition to the A/Wisconsin/67/2005-like (H3N2) and B/Malaysia/2506/2004-like viruses, A/Solomon Islands/3/2006 (H1N1) is a new viral strain in the TIV for 2007-2008.
- Due to widespread resistance, amantadine and rimantadine are no longer recommended for the treatment or chemo-prophylaxis of influenza A in the United States; instead, neuraminidase inhibitors should be considered.

For additional information, please visit: [www.cdc.gov/flu/professionals/acip/index.htm](http://www.cdc.gov/flu/professionals/acip/index.htm)

# Advisories

## Children's Cough and Cold Medicines

On 10/11/2007, drug companies agreed to voluntarily withdraw OTC cough and cold medicines for infants and toddlers <2 years of age, following warnings of potential health risks. The voluntary withdrawal did not include products for children >2, despite warnings that the products may pose health risks in children up to 6 years of age. The serious adverse event reports are primarily believed to be a result of children receiving medication overdoses; however, the overall benefit:risk ratio of these agents remains controversial.

## Avandia® (rosiglitazone)

On 11/14/2007, the FDA announced the addition of new information regarding the potential for increased risk of heart attacks to the existing boxed warning

following the finding of increased myocardial ischemic events in a meta-analysis of 42 clinical studies most of which compared rosiglitazone to placebo. There is insufficient evidence available at this time to compare the safety of rosiglitazone with other oral type 2 diabetes treatments.

## Prilosec® (omeprazole) and Nexium® (esomeprazole)

On 10/11/2007, the FDA announced the completion of a comprehensive review of safety data for omeprazole and esomeprazole. Based on available evidence, there does not appear to be an increased frequency of heart attacks and other heart-related problems attributable to the drugs. Therefore, the FDA concluded that long-term use of these agents is unlikely to be associated with an increased risk of heart problems.

## DDAVP® Nasal Spray, DDAVP® Rhinal Tube, DDAVP®, DDVP®, Minirin® and Stimat® Nasal Spray (desmopressin acetate)

On 12/4/2007, the FDA issued an alert regarding an increased risk for developing severe hyponatremia that may lead to seizures and death. Children treated with intranasal formulations for primary nocturnal enuresis (PNE) appear to be at the greatest safety risk. As such, intranasal formulations should not be used for the treatment of PNE nor in patients with hyponatremia or a history of hyponatremia. Additionally, PNE treatment with desmopressin tablets should be discontinued during acute illnesses that may lead to fluid and/or electrolyte imbalances.



## From The Hill

### Federal

#### Communicating Off-label Research: The FDA Considers Changing Restrictions on Drug Marketing

The FDA is considering allowing pharmaceutical manufacturers to provide prescribers with medical studies of unapproved uses for drugs. More specifically, the guidance would outline criteria for the dissemination of “truthful and non-misleading” journal reprints and other publications on unapproved uses of approved drugs and devices to healthcare professionals. Critics argue that the long standing restrictions on the marketing of drugs and medical devices should be upheld. A temporary exception was created in 1997 and allowed manufacturers to circulate literature reprints, as long as the documents were submitted to the FDA in advance and were subsequently approved. However, this exception expired in 2006, and the new guidance is currently being drafted by the FDA.

For more information, please visit: [www.kaisernetwork.org/daily\\_reports/rep\\_index.cfm?DR\\_ID=49174](http://www.kaisernetwork.org/daily_reports/rep_index.cfm?DR_ID=49174) and [www.mmm-online.com/Waxman-FDA-off-label-reprint-guidance-on-the-way/article/99487/](http://www.mmm-online.com/Waxman-FDA-off-label-reprint-guidance-on-the-way/article/99487/)

### State

**Massachusetts:** The budget for fiscal year 2008 authorizes the following: a CMS Medicaid Transformation Grant which funds a MassHealth e-Prescribing pilot project; the state Health Care Financing agency to change the pricing for generic and multiple-source drugs; funding for the Prescription Advantage state pharmaceutical assistance programs or “SPAPs;” funding for Medicaid’s dual-eligible pharmaceutical “clawback” payment; and payments to community health centers for pharmaceutical services provided to uninsured individuals.

**Vermont:** Newly passed legislation will limit the “fraudulent” advertising of prescription drugs. More specifically, this legislation will increase the “transparency of prescription drug pricing and information.”

# Pipeline

## Intuniv® (guanfacine)

Shire received an approvable letter from the FDA for guanfacine extended release tablets, a nonstimulant selective alpha-2A-receptor agonist. Shire is seeking FDA approval as monotherapy for the treatment of ADHD symptoms throughout the day in children 6 to 17 years old.

## SPD465 (mixed amphetamine salt formulation)

Shire received an approvable letter from the FDA for a single entity, mixed amphetamine salt formulation. SPD465 is currently under FDA review for symptom control for up to 16 hours in adults with ADHD.

# Noteworthy

## FDA Against Approving an OTC Statin

On 12/13/07, FDA advisors recommended against approving over-the-counter Mevacor® (lovastatin) by means of a 10-2 vote with one abstention. The panel voted 11-2 that the consumer behavior study conducted by Merck for the lovastatin 20mg switch application was unable to demonstrate consumers could make an appropriate self-selection decision. The committees voted, 12-1, against consumer understanding of the proposed label warning concerning muscle pain, but 9-3 with one abstention that the application supports adequate consumer understanding of the label warning concerning pregnancy.

## What's New at CPS?

Clinical Pharmacy Services (CPS) has begun the development and expansion of additional clinical programs including Retrospective Drug Utilization Review (RetroDUR), Medication Therapy Management (MTM), and Disease State Management (DSM). In January 2008, CPS will launch new MTM and RetroDUR programs including disease specific programs for asthma, congestive heart failure, and post-myocardial infarction. Programs focusing on the treatment of other chronic diseases are currently under development.

Additional program details and selected initiatives will be discussed in future issues of the CPS Insider.



## UMMS Clinical Pharmacy Services: Who We Are and What We Do

The University of Massachusetts Medical School (UMMS) Clinical Pharmacy Services (CPS) is a comprehensive prescription drug management program developed in 1999 as part of UMMS' Commonwealth Medicine division, primarily to provide drug utilization review for Massachusetts Medicaid. Today, CPS brings exceptional depth and experience in the development and implementation of unique, client-customized managed care-related clinical pharmacy functions including, but not limited to, evidence-based formulary support, drug utilization review, medication therapy management, clinical call center support and provider/patient education. 'CPS Insider' is an educational resource produced quarterly in an effort to deliver critical information at the highest level of quality to our clients. We hope that you find this resource of value and welcome your suggestions for improvement.



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